Vaccine 32 (2014) 284–289

Contents lists available at ScienceDirect

Vaccine

journal homepage: www.elsevier.com/locate/vaccine

Timeliness of infant vaccination and factors related with delay in Flanders, Belgium

Tinne Lernout[a,*,1], Heidi Theeten[a,b,1], Niel Hens[c,d], Tessa Braeckman[a], Mathieu Roelants[e], Karel Hoppenbrouwers[e], Pierre Van Damme[a]

[a] Centre for the Evaluation of Vaccination, Vaccine and Infectious Disease Institute, University of Antwerp, Antwerp, Belgium
[b] Post-doctoral Research Fellow of the Fund of Scientific Research (FWO), Belgium
[c] Centre for Health Economic Research and Modelling Infectious Diseases, Vaccine and Infectious Disease Institute, University of Antwerp, Antwerp, Belgium
[d] Interuniversity Institute for Biostatistics and statistical Bioinformatics, Hasselt University, Diepenbeek, Belgium
[e] Centre for Youth Health Care, Department of Public Health and Primary Care, KU Leuven, University of Leuven, Belgium

ARTICLE INFO

Article history:
Received 12 September 2013
Received in revised form 23 October 2013
Accepted 24 October 2013
Available online 16 November 2013

Keywords:
Infant vaccination
Timeliness
Risk factors
Flanders

ABSTRACT

Achieving high vaccination coverage is a necessary, but not a sufficient indicator of the quality of a vaccination programme, in terms of control and prevention of childhood infectious diseases. For optimal protection of infants, timeliness of vaccination is increasingly recognized as another important target.

The aim of this study was to assess the timeliness of measles-mumps-rubella (MMR) and diphtheria-tetanus-pertussis (DTP) vaccination in infants in Flanders (Belgium), and to identify predictors of vaccination delay. The timeliness was assessed using the Kaplan–Meier estimator in three consecutive vaccination coverage surveys among children aged 18–24 months, conducted in 2005, 2008 and 2012, respectively. Factors associated with delayed administration of the vaccines were identified using Cox regression analysis.

Over the time period, vaccination coverage for the first dose of MMR ranged from 94.0 to 96.6% and for the third dose of DTP from 97.9 to 98.7%. However, up to 32% (for MMR1) and 95% (for DTP3) of infants received vaccine doses delayed according to the recommended schedule. Although some improvement was achieved over the last decade, further efforts are needed to reach risk groups with delays, more specifically children vaccinated outside the baby well clinics, born from a mother originating from outside the European Union, children with a higher ranking or in families with a lower income.

© 2013 Elsevier Ltd. All rights reserved.

1. Introduction

To achieve effective control of vaccine-preventable infectious diseases, a high coverage with efficacious vaccines is a prerequisite. The global target of the World Health Organization (WHO) for the vaccination coverage in infants is 90% [1]. For the elimination of measles and rubella, which is an additional goal in the American and European WHO regions, an even higher coverage is required [2].

In addition to obtaining high coverage, timely vaccination is of critical importance for reducing disease risk. Delayed infant vaccination enlarges the gap between loss of protection from maternal antibodies and full protection from vaccine-induced immunity, negatively affects herd immunity and postpones full protection in infants and children. As a consequence, infants are longer vulnerable to vaccine preventable diseases, such as Bordetella pertussis and measles, contributing to outbreaks of the latter in various countries [3,4].

Vaccination coverage is the most frequently used indicator for the evaluation and monitoring of vaccination programmes. However, age-specific infant vaccination coverage, e.g. at the age of 18–24 months, provides no information on possible delays of vaccine-administration. Timely vaccination can be assessed from cross-sectional survey data through a time-to-event analysis using the Kaplan–Meier estimator [5–8].

Recommendations on the Belgian infant immunisation schedule are published by the national Superior Health Council (SHC) [9]. In Flanders, the northern region of Belgium which represents about 60% of the population, surveys repeatedly showed high coverage estimates for vaccines recommended in infancy. In 2012, coverage rates were ≥92% for all infant vaccinations, and above 95% for the first dose of measles-mumps-rubella vaccine (MMR1) [10]. Infant vaccines are mostly administered at well baby clinics (under-5

* Corresponding author at: Centre for the Evaluation of Vaccination, Vaccine and Infectious Disease Institute, University of Antwerp, Universiteitsplein 1, B-2610 Antwerp, Belgium. Tel.: +32 3 265 28 61.
E-mail address: tinne.lernout@uantwerpen.be (T. Lernout).
[1] Contributed equally.

0264-410X/$ – see front matter © 2013 Elsevier Ltd. All rights reserved.
http://dx.doi.org/10.1016/j.vaccine.2013.10.084

clinics) (83.7% of vaccines in 2012), or by a family physician or paediatrician (15.6%).

The current study focuses on adherence to age recommendations for infant vaccination against measles and pertussis, since both diseases have caused infant cases in Flanders recently, despite high vaccination coverage [11–13]. The study also aimed to detect trends over 3 coverage studies in the past 7 years, and to identify subpopulations of infants who are at higher risk for delayed vaccination.

2. Methods

2.1. Study population and survey design

The present study is based on data from three cross-sectional EPI-surveys, conducted in 2005, 2008 and 2012 in Flanders [10,14,15]. Each survey used the same study design. Infants 18–24 months of age were selected with a two-stage random cluster design. First, 125 clusters (municipalities) spread over the 5 provinces in Flanders were randomly selected with proportionate probability to their size. In each cluster, the requested number of children were then randomly selected from the National register of residents. Sample sizes were calculated based on the latest available coverage rates for each study, considering a design effect of 1.5 (2008, 2012)–2 (2005), a margin error of the confidence interval of 2.5% and a drop-out rate of 10%. The number of participants was 1354 in 2005 (participation rate 92.2%), 915 in 2008 (91.3%) and 874 (92.4%) in 2012.

The design and methods of these studies have been described in detail elsewhere [10,14,15]. In summary, parents or caregivers were visited at home by a professional interviewer, trained on the questionnaire and interpretation of vaccination data by the researchers.

Immunisation dates were transcribed from vaccination cards and completed or validated through Vaccinnet, the electronic vaccine ordering and registration system set up in Flanders in 2006 (for the 2008 and 2012 surveys) [16]. Further missing data were completed with information in medical files, as far as they could be consulted. Demographical data (age of the child, gender, rank within the family and number of siblings, number of past illness episodes) and socio-economic characteristics of the parents (family income, single parentage, parental age, employment status, educational level and ethnicity) were collected through a structured interview. The main vaccinating physician (well baby clinic, paediatrician, family physician) was defined as the one who had administered the majority of vaccine doses. Each survey was approved by the respective ethics committees of all universities involved and by the privacy commission of the Belgian Government. Written informed consent was obtained from a parent or legal guardian of each infant included in the study.

2.2. Outcome measures

In a first analysis, vaccinated children were classified by the level of delay in vaccination for MMR1 and the three doses of diphtheria-tetanus-pertussis (DTP1, DTP2, DTP3), according to the schedule recommended by the SHC. The recommended age of vaccination for MMR1 in Belgium is 12 months of age, and DTP doses are recommended at 8, 12 and 16 weeks (2, 3 and 4 months in 2005).

Time-to-event analysis was used to further analyse the age at administration and risk factors for delayed vaccination for the vaccines studied.

First, a Kaplan–Meier survival analysis was applied to the 2005, 2008 and 2012 surveys to estimate the age-specific coverage rates and 95% confidence intervals with censoring of children who had not yet received the respective dose at the time of the interview (for 2005, the start of the study was used because the interview date was not registered) [6]. The response of interest was time to vaccination, which was calculated in weeks. Timely vaccination was defined as occurring within 6 days of the recommended age for DTP and 30 days for MMR1.

In a second step, risk factors for delayed vaccination were identified using a Cox proportional hazard (PH) regression model. We opted to use continuous time-to-event analysis and not to categorize delay of vaccination, since categorizing would impact on the associations and up to now there is insufficient evidence to state which level of delay impairs vaccine effectiveness. The hazard expresses the rate for a child to be vaccinated at a specific moment in time. Reciprocal hazard ratio (1/HR) was used to present a higher risk to be vaccinated at a later age compared to the reference group (if HR > 1). Cox PH regression models used the socio-demographic variables from the interview as possible predictors. To avoid co-linearity for parental characteristics, only maternal factors were included in the analysis (except when only information on the father was available).

2.3. Statistical analysis

Cluster effects arising from the sample design were controlled for using the method developed by Ying and Wei [17,18]. The validity of the proportional hazard assumption, which is a condition for Cox regression analysis, was evaluated using Schoenfeld residuals [19]. Variables were omitted by backward stepwise selection, based on significance level (p-value > 0.1). Associations were considered statistically significant if the p-value was <0.05. Kaplan–Meier analysis was performed using SPSS 20.0 and R 2.15.1 was used for the Cox regression analysis.

3. Results

3.1. Timeliness of vaccination

Respectively 62%, 69% and 72% of infants received MMR1 before the age of 13 months (56 weeks) in 2005, 2008 and 2012 (Table 1). The largest reduction in delay over the 7 years study period was observed for doses administered more than 2 months after the recommended age.

Recommendations for administration of pertussis containing vaccines (DTP) are less well followed. The majority of children were vaccinated with a delay of 1–4 weeks, and the delay increases for subsequent doses, up to more than 2 months for 10% of DTP3 vaccinations. However, the proportion of timely administered doses also increases over the study period, especially for DTP1.

3.2. Coverage by age from Kaplan–Meier analysis

Estimates of vaccination coverage by age (inverse survival curves) were plotted in Fig. 1. The curves for DTP1 and DTP2 were similar to those for DTP3 and are not presented.

An MMR1 coverage of 95% was reached at 99 weeks of age in 2005, 77 weeks in 2008 and 75 weeks in 2012. The 2008 and 2012 plots show a higher maximum and a more outspoken rectangular shape compared to the 2005 graph, which reflects a higher adherence to age recommendations.

Coverage by age for DTP3 reached 95% at 38, 32 and 30 weeks of age in the consecutive studies. A small improvement in adherence to age recommendations for DTP3 vaccination is observed between 2005 and 2008, but not anymore from 2008 to 2012.

Table 1
Vaccination coverage and timeliness of administration for MMR and DTP vaccines in children 18–24 months in Flanders, 2005, 2008 and 2012 (in % of total number of children).

Vaccine	Year	Coverage 18–24 months (95% CI)	Not delayed	1–4 weeks too late	1–2 months too late	>2 months too late
MMR1	2005	94.0 (92.6–95.3)	61.6	NA	22.1	10.3
	2008	96.6 (95.2–97.6)	69.2	NA	20.7	6.8
	2012	96.6 (95.1–97.6)	72.4	NA	19.3	4.9
DTP1	2005	98.7 (98.1–99.3)	23.7	64.3	6.9	3.8
	2008	99.3 (98.5–99.7)	25.2	68.7	3.2	2.2
	2012	99.5 (98.7–99.8)	37.8	56.4	3.4	1.9
DTP2	2005	98.2 (97.4–99.0)	8.4	71.1	12.7	6.0
	2008	98.6 (97.6–99.2)	9.0	77.0	9.1	3.5
	2012	99.1 (98.2–99.6)	15.3	69.8	9.7	4.3
DTP3	2005	97.9 (97.0–98.8)	2.9	60.8	21.6	12.6
	2008	98.3 (97.2–98.9)	3.6	61.4	23.2	10.1
	2012	98.7 (97.6–99.3)	6.4	61.7	19.3	11.3

N = 1354 in 2005, 915 in 2008 and 874 in 2012.
Not delayed = within 6 days of the recommended age for DTP1-3 and 30 days for MMR1.

3.3. Factors related with delayed administration

The main determinants of age of administration of DTP and/or MMR vaccines in the 2012 survey were the infants' rank in the family, the mother's origin, the family income and the main vaccinator (Table 2). The results for DTP2 were comparable to those for DTP3 and are not presented.

Children were vaccinated at a later age when vaccinated outside a well baby clinic, when their mother was born outside the European Union or when their birth order was higher (except for DTP1). Having a younger mother was also associated with delayed vaccination, although the effect was limited. A lower family income was associated with delayed DTP3 vaccination only. For both MMR and DTP, the strongest association was found with the main vaccinator.

The child's province of residence, gender, number of past illness episodes, possible switch between vaccinators during the vaccination course as well as the mother's level of education and employment status did not significantly influence the age of vaccination.

Results from the 2005 and 2008 surveys (not shown) confirmed the influence of the main vaccinator and the child's rank in the family as the most important characteristics associated with delay, as well as an association with the age of the mother.

4. Discussion

4.1. Timely administration of vaccines

Several recent studies highlighted the need of assessing timeliness of vaccination in addition to measuring up-to-date vaccination coverage since simply considering immunisation levels at a given age may overestimate protection in the population of interest

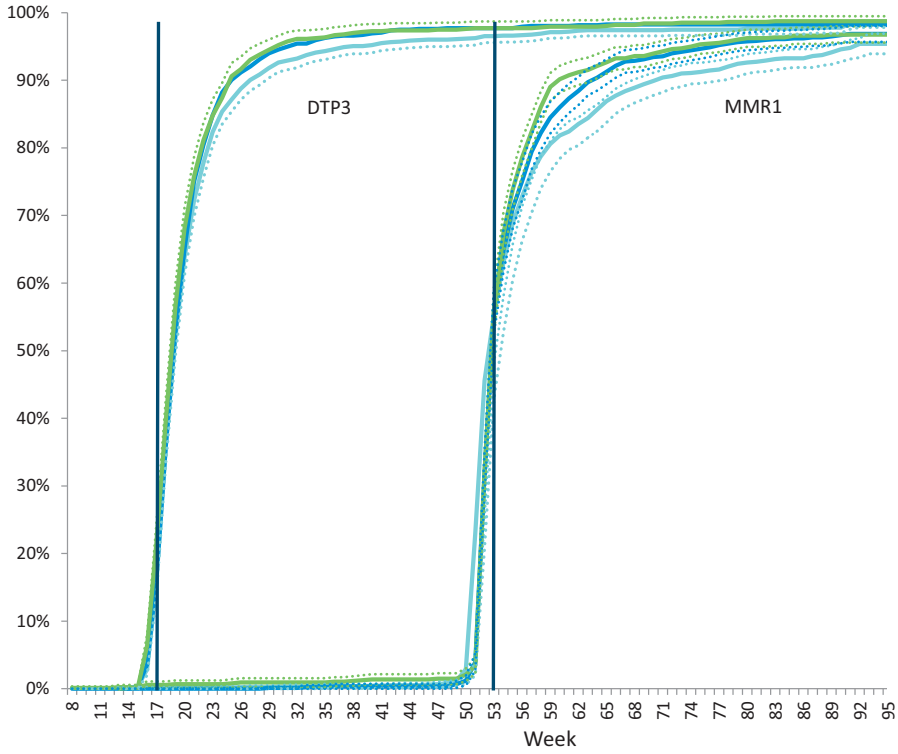

Fig. 1. Age-related coverage for DTP3 and MMR1 vaccines in the study cohorts, Flanders, 2005, 2008 and 2012.

Table 2
Hazard ratio's (and 95% CI) for delayed vaccination according to determining factors (Cox proportional hazard regression, final models) for DTP1, DTP3 and MMR1, Flanders, 2012.

Determining factor	Subcategory	DTP1	DTP3	MMR1
Child's rank	Single		1	1
	First		0.99 (0.76–1.28)	1.05 (0.81–1.36)
	Second		1.07 (0.90–1.26)	**1.29 (1.09–1.52)****
	Third		**1.42 (1.12–1.80)****	**1.56 (1.22–1.98)*****
	4th or higher		**1.47 (1.05–2.06)***	**2.28 (1.61–3.22)*****
Family	2 biological parents			1
	Single or reconstituted			1.30 (0.95–1.78)
Mother's age (increasing)			**0.98 (0.97–0.99)***	**0.98 (0.97–0.99)***
Mother's origin	Belgium	1	1	1
	Other EU	1.14 (0.86–1.51)	0.94 (0.70–1.25)	0.90 (0.67–1.21)
	Outside EU	**1.40 (1.17–1.69)*****	**1.29 (1.04–1.59)***	**1.29 (1.07–1.57)****
Family income	<1500€		1	
	1500–2000€		0.87 (0.60–1.29)	
	2001–3000€		**0.64 (0.46–0.88)****	
	>3000€		**0.63 (0.46–0.87)****	
	Unknown		0.90 (0.60–1.33)	
	Refused to mention		0.74 (0.50–1.11)	
Main vaccinator	Well baby clinic	1	1	1
	Paediatrician	1.08 (0.87–1.34)	**1.37 (1.10–1.71)****	**1.98 (1.58–2.48)*****
	General practitioner	**2.12 (1.44–3.13)*****	**1.97 (1.34–2.90)*****	**2.54 (1.69–3.82)*****
	Outside Flanders	**2.72 (1.10–6.71)***	2.47 (1.00–6.12)	**3.36 (1.21–9.32)***

HR printed in bold are significant with $^{*}p < 0.05$; $^{**}p < 0.01$; $^{***}p < 0.001$.
EU, European Union.

[7,20,21]. Coverage rates of 95% estimated at 18–24 months of age might not be sufficient to assure adequate protection of infants, especially for pertussis and measles. This is also the case in Flanders, although we could demonstrate that rising infant coverage was associated with increasing timeliness of vaccination.

Based on survey data from children born in 2003, 2006 and 2010, we showed that timely administration of MMR vaccinations in infancy increased with 10% over the last decade in Flanders. This evolution might partially be the result of increased attention for timely vaccination in well baby clinics in Flanders, as well as awareness campaigns conducted in Flanders, such as the European Immunisation Week in 2008, which was entirely dedicated to measles vaccination. However, measles is still a cause of concern in Belgium [11,12] and the timeliness could achieve higher levels if further efforts are made for those children vaccinated with a delay of 1–2 months only. Reaching 95% vaccination coverage as early as possible in the young population might be a step forward to measles elimination [2]. From the age of 6 months up to their second birthday, children in a study cohort in Switzerland, where measles outbreaks occurred in the last decade, spent on average 266 days unvaccinated and susceptible to measles. One third of these 266 days was due to delayed vaccination [20].

Adherence to the age recommendations is harder to achieve for DTP than for MMR since these recommendations are much stricter (within 6 days). This is reflected in higher proportions of infants with delayed immunisation and markedly lower timeliness for consecutive doses. Furthermore, little improvement was achieved the last decade. Respectively 2.9%, 3.6% and 6.4% of infants received DTP3 before or at the recommended age of 16 weeks (+6 days) in 2005, 2008 and 2012. Although the incidence of pertussis showed a decreasing trend in Belgium since 2007, there is still circulation of the disease, as is illustrated by an increasing number of reported cases through mandatory notification in Flanders in 2012 [12,13]. Among the 42 infant cases reported that year, 57% were 3–11 months old. Timely vaccination, is therefore increasingly important.

Age-appropriate vaccination reported in several studies in low and middle-income countries varies substantially, with delayed vaccination ranging from 19 to 78% for the first dose of measles containing vaccines (MCV1), and from 18 to 90% for pertussis containing vaccines [22–25]. However, definition of delay is not consistent and recent reports on timing of infant vaccinations in high-income countries are rare. A study in Switzerland reports delayed vaccination for MCV1 in 22% of vaccinated infants, comparable to what is observed in Flanders, but with a low vaccination coverage (62.6%) [20]. No data are comparable to our study for pertussis containing vaccines. The results presented here illustrate that timely vaccination is an issue even in high income countries with high coverage.

Reducing delay and aiming for infant immunisation at the earliest appropriate age in Flanders was prioritized after the 2005 survey, when high levels of coverage had been reached. Timely vaccination is an explicit goal for "Child and Family" (Kind & Gezin), the main supporting organisation of the well baby clinics in Flanders. They have made active efforts to enhance timeliness, mainly by raising awareness of nurses and physicians and by sending reminders through email or telephone (SMS), but are currently limited by the capacity of their services.

4.2. Risk factors for remaining delay

Despite the achievement of high coverage rates and the increased adherence to recommended age of administration, further improvement of timely vaccination remains an important goal in Flanders. Several risk factors for delay were identified in our study, the main ones being vaccinated outside well baby clinics and having a mother originating from outside the European Union. A higher ranking of the child within the family and a lower income were risk factors for some of the vaccines or doses studied. Both were also identified as risk factors for delayed vaccination in a study in 31 low and middle income countries, in Uganda and in the US [22,23,26]. Special attention is thus needed for children born in larger families or with origins outside Europe as well as for children vaccinated outside well baby clinics. In addition, delay due to illness or logistic reasons should be limited and well followed up through an efficient reminder system. In a study in the US, 60% of children

with missed vaccine opportunities did not receive age-appropriate immunisations within 6 months [27]. Sufficient vaccine supply at private physician's offices is essential to avoid delayed vaccination. This might improve in 2014, when the use of Vaccinnet will be mandatory for ordering free of charge vaccines in Flanders, allowing an efficient delivery of the vaccines at private practices as well. This electronic vaccination database could also be used to identify children with missing doses and recall them for vaccination in a timely way, as is the case in some other immunisation information systems (IIS) [28]. Furthermore, since timely vaccination scores higher in well baby clinics, sufficient resources should be allocated to these clinics, to ensure a continuous and adequate service to the population.

Finally, emphasizing the importance of timeliness is needed in the communication to parents as well as physicians.

4.3. Limitations of the study

When using time-to-event analysis, we assumed that any dose which was not yet given at the moment of the interview was in fact a delayed dose, which could still be given at any time after the interview. Because of this assumption, we cannot exclude that part of the gain in timeliness was due to improving access to computerized vaccination data. Increased use over the study time period of Vaccinnet allowed better documentation of vaccines administered at well baby clinics and by private physicians, which are increasingly registering vaccinations in this system since 2006 [16]. However, this effect is limited since in each survey intense efforts were made to retrieve additional data from medical files.

The Cox regression we used, identified factors related with "an older age at vaccination", comparing with the mean age at vaccination in the reference group. A multiple regression analysis on the 2012 survey data that evaluated risk factors for being not (yet) fully vaccinated at 18 months of age, corresponding to a considerable delay for any of the studied vaccines, identified ranking (or number of children), mother's age and main vaccinator as determinants, similar to the results in this study (not shown) [10].

5. Conclusions

Routine evaluation of vaccination programmes is based on measuring vaccine uptake (vaccine coverage), however relying only on vaccination coverage may mask important delays in vaccination and subsequent lack of immunity, leading to a false assumption of disease protection.

Our data demonstrate that compliance to recommendations on timing of infant vaccines in Flanders increased over the past decade. Nevertheless, further improvement is necessary, especially for DTP, to optimize control of pertussis. This is possible through targeting infants who are at risk for delay. The barriers contributing to delay in vaccination and possible measures to improve timeliness identified in our study may also apply to similar settings in other European countries.

Conflict of interest statement

The coverage surveys received full funding from the Flemish government, and were commissioned by the Flemish Minister in charge of the health policy. NH was partly funded by the Scientific Chair in Evidence-based Vaccinology sponsored in 2009–2014 by an unrestricted gift from Pfizer. PVD and KH have been principal investigator of vaccine trials for several vaccine manufacturers for which the respective universities obtained research grants. All other authors have no competing interests to declare.

Acknowledgements

We thank all the families who participated in the surveys, as well as the physicians who supplied information from their files. The vaccination coverage surveys were funded by the Flemish government. NH acknowledges "SIMID", a strategic basic research project funded by the institute for the Promotion of Innovation by Science and Technology in Flanders (IWT), project number 060081; the Chair in Evidence-based Vaccinology was sponsored in 2009–2014 by an unrestricted gift from Pfizer and the IAP research network number P6/03 of the Belgian Government (Belgian Science Policy).

References

[1] World Health Organization. WHO Global Immunisation Vision and Strategy 2006–2015. Available at http://www.who.int/vaccines-documents/DocsPDF05/GIVS_Final_EN.pdf
[2] World Health Organization. Eliminating measles and rubella and preventing congenital rubella infection: WHO European Region strategic plan 2005–2010. Available at http://www.euro.who.int/_data/assets/pdf_file/0008/79028/E87772.pdf
[3] Siedler A, Hermann M, Schmitt HJ, Von Kries R. Consequences of delayed measles vaccination in Germany. Pediatr Infect Dis J 2002;21(9):826–30.
[4] Park YJ, Eom HS, Kim ES, Choe YJ, Bae GR, Lee DH. Reemergence of measles in South Korea: implications for immunisation and surveillance programs. Jpn J Infect Dis 2013;66(1):6–10.
[5] Laubereau B, Hermann M, Schmitt HJ, Weil J, Von Kries R. Detection of delayed vaccinations: a new approach to visualize vaccine uptake. Epidemiol Infect 2002;128(2):185–92.
[6] Dayan GH, Shaw KM, Baughman AL, Orellana LC, Forlenza R, Ellis A, et al. Assessment of delay in age-appropriate vaccination using survival analysis. Am J Epidemiol 2006;163(6):561–70.
[7] Akmatov MK, Kretzschmar M, Kramer A, Mikolajczyk RT. Timeliness of vaccination and its effects on fraction of vaccinated population. Vaccine 2008;26(31):3805–11.
[8] Clark A, Sanderson C. Timing of children's vaccinations in 45 low-income and middle-income countries: an analysis of survey data. Lancet 2009;373(9674):1543–9.
[9] Superior Health Council. Recommended vaccination schedule; 2009. Available at http://www.health.belgium.be/internet2Prd/groups/public/@public/@shc/documents/ie2divers/4938405.pdf [Dutch].
[10] P. Van Damme, H. Theeten, T. Braeckman, T.Lernout, N. Hens, K. Hoppenbrouwers et al. Vaccination coverage survey in infants and adolescents in Flanders in 2012. Available at http://www.zorg-en-gezondheid.be/vaccinatiegraad [Dutch].
[11] Braeye T, Sabbe M, Hutse V, Flipse W, Godderis L, Top G. Obstacles in measles elimination: an in-depth description of a measles outbreak in Ghent, Belgium, spring 2011. Arch Public Health 2013;71(July (1)):17.
[12] Scientific Institute of Public Health (WIV-ISP). Vaccine preventable infectious diseases in children. In: Trends and evolution in Belgium; 2011. Available at https://www.wiv-isp.be/pedisurv/AnnualReports/2011/jaarverslag_2011_nl.pdf [Dutch].
[13] De Schrijver K, Voeten M, Van den Branden D, Boeckx H, Dierckx E, Wojciechowski M, et al. Does pertussis increase in Flanders and is health staff involved in the transmission? Vlaams Infectieziektenbulletin 2013;3:5–11 [Dutch].
[14] Boonen M, Theeten H, Vandermeulen C, Roelants M, Depoorter A, Van Damme P, et al. Vaccination coverage in infants and adolescents in Flanders in 2008. Vlaams Infectieziektenbulletin 2009;68(2):9–14 [Dutch].
[15] Theeten H, Hens N, Vandermeulen C, Depoorter AM, Roelants M, Aerts M, et al. Infant vaccination coverage in 2005 and predictive factors for complete or valid vaccination in Flanders, Belgium: an EPI-survey. Vaccine 2007;25(26):4940–8.
[16] Top G, Paeps A, Wildemeersch D. Vaccinnet, a vaccine ordering system linked to a vaccination database in Flanders, Belgium. In: Poster Eurovaccine. 2009.
[17] Ying Z, Wei LJ. The Kaplan–Meier estimate for dependent failure time observations. J Multivariate Anal 1994;50:17–29.
[18] Chuang SK, Tian L, Wei LJ, Dodson TB. Kaplan–Meier analysis of dental implant survival: a strategy for estimating survival with clustered observations. J Dent Res 2001;80(11):2016–20.
[19] Therneau T, Grambsch P. Modelling survival data. Springer; 2000.
[20] Bielicki JA, Achermann R, Berger C. Timing of measles immunisation and effective population vaccine coverage. Pediatrics 2012;130(September (3)):e600–6.
[21] Poorolajal J, Khazaei S, Kousehlou Z, Bathaei S, Zahiri A. Delayed vaccination and related predictors among infants. Iran J Public Health 2012;41(10):65–71.
[22] Akmatov MK, Mikolajczyk RT. Timeliness of childhood vaccinations in 31 low and middle-income countries. J Epidemiol Community Health 2012;66(July (7)):e14.
[23] Babirye JN, Engebretsen IM, Makumbi F, Fadnes LT, Wamani H, Tylleskar T, et al. Timeliness of childhood vaccinations in Kampala Uganda: a community-based cross-sectional study. PLoS ONE 2012;7(4):e35432.
[24] Le Polain de Waroux O, Schellenberg JR, Manzi F, Mrisho M, Shirima K, Mshinda H, et al. Timeliness and completeness of vaccination and risk factors for low

and late vaccine uptake in young children living in rural southern Tanzania. Int Health 2013;5(June (2)):139–47.
[25] Ettarh RR, Mutua MK, Kyobutungi C. Ethnicity and delay in measles vaccination in a Nairobi slum. Trop Med Health 2012;40(June (2)):59–62.
[26] Luman ET, McCauley MM, Stokley S, Chu SY, Pickering LK. Timeliness of childhood immunisations. Pediatrics 2002;110(November (5)): 935–9.
[27] Sabnis SS, Pomeranz AJ, Lye PS, Amateau MM. Do missed opportunities stay missed? A 6-month follow-up of missed vaccine opportunities in inner city Milwaukee children. Pediatrics 1998;101(May (5)):E5.
[28] Braeckman T, Lernout T, Top G, Paeps A, Roelants M, Hoppenbrouwers K, et al. Assessing vaccination coverage in infants, survey studies versus the Flemish immunisation register: achieving the best of both worlds. Vaccine 2013. Nov 20.